Perspective – *Molecular Ecology*

Introgressive hybridization: brown bears as vectors for polar bear alleles

FRANK HAILER [1,2]

[1] *Organisms and Environment Division, School of Biosciences, Cardiff University, Cardiff CF10 3AX, Wales, UK*

[2] *Biodiversity and Climate Research Centre (BiK-F), Senckenberg Research Institute, Senckenberganlage 25, 60325 Frankfurt am Main, Germany*

Correspondence: Frank Hailer, Email: frashai@gmx.net

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The dynamics and consequences of introgression can inform about numerous evolutionary processes. Biologists have therefore long been interested in hybridization. One challenge, however, lies in the identification of non-admixed genotypes that can serve as a baseline for accurate quantification of admixture. In this issue of *Molecular Ecology*, Cahill *et al.* (2014) analyze a genomic data set of 28 polar bears, eight brown bears and one American black bear. Polar bear alleles are found to be introgressed into brown bears not only near a previously identified admixture zone on the Alaskan Admiralty, Baranof, and Chichagof (ABC) Islands, but also far into the North American mainland. Elegantly contrasting admixture levels at autosomal and X-chromosomal markers, Cahill and colleagues infer that male-biased dispersal has spread these introgressed alleles away from the late Pleistocene contact zone. Compared to a previous study on the ABC Island population in which an Alaskan brown bear served as a putatively admixture-free reference, Cahill *et al.* (2014) utilize a newly sequenced Swedish brown bear as admixture baseline. This approach reveals that brown bears have been impacted by introgression from polar bears to a larger extent (up to 8.8% of their genome), than previously known, including the bear that had previously served as admixture baseline. No evidence for brown into polar bear introgression is found, which the authors argue could be a consequence of selection. Besides adding new exciting pieces to the puzzle of polar/brown bear evolutionary history, the study by Cahill and colleagues highlights that wildlife genomics is moving from analyzing single genomes towards a landscape genomics approach.

Genomic studies are revealing a wealth of information about past evolutionary events. For instance, we are gaining insights into the dynamic nature of species integrity over time, and how factors like climate and demography have influenced the coexistence and adaptation of differentiated phenotypes.

For studies of introgression, the presence of a pure, non-admixed genotype is required as a baseline for accurate estimation of admixture rates. In human genetics research, relatively admixture-free populations from sub-Saharan Africa have been used to quantify Neanderthal admixture in our genomes, and populations from outside Asian and Oceania for quantification of Denisovan ancestry (Sánchez-Quinto & Lalueza-Fox 2015). However, such information is lacking for most study systems, complicating the quantification of admixture levels.

Polar and brown bears and their history of admixture on the Alaskan ABC Islands

Polar and brown bears are sister species whose evolutionary histories are intertwined by introgressive hybridization and incomplete lineage sorting (ILS). Recently, Cahill *et al.* (2013) used extensive demographic modeling to demonstrate that the genomes of brown bears on the ABC Islands derive from a Pleistocene polar bear population that over time received extensive male-biased gene flow from mainland brown bears. This process has retained only a small proportion of polar bear alleles on the ABC Islands, with a gradual conversion into a brown bear-like genotype and phenotype.

In this issue of *Molecular Ecology*, Cahill *et al.* (2014) add three brown bear genomes to other recently sequenced bear genomes, mining the data for signals of admixture using D and $\hat{f}$-statistics (ABBA/BABA tests; Green *et al.* 2010; Durand *et al.* 2011). Utilizing a newly sequenced Swedish brown bear as a baseline, Cahill *et al.* (2014) report 5.9-8.8% of polar bear ancestry on the autosomes and 7.5-9.7% on the X chromosomes of five ABC-Islands brown bears. Interestingly, the brown bear from Admiralty Island that was analyzed in both studies (Cahill *et al.* 2013, 2014) now shows much higher polar bear ancestry (autosomes: 6.0%, X-chromosome: 7.6%) than in the previous study (autosomes: <1%, X-chromosome: 6.5%) when using an Alaskan brown bear as admixture-free reference. The new baseline also reveals that the Alaskan mainland brown bear individual that was previously used as an admixture baseline (Cahill *et al.* 2013) in fact shows clear signals of polar bear introgression. This bear shows a reversed discordance in admixture levels between the autosomes and the X chromosome compared to ABC Island bears: on the mainland, introgression is lower on the X than on the autosomes, which can be explained by male-biased dispersal not only *to* but also *from* the ABC Islands. Hence, based on different contributions of male or female dispersers to the gene pool of autosomes and X chromosomes, (Cahill *et al.* 2013, 2014) recover a fascinating evolutionary history of ABC Islands bears: male brown bears bringing brown bear alleles onto the islands, and male bears also dispersing off the islands – carrying some polar bear alleles onto the continent. Last but not least, the present study by Cahill and colleagues highlights that the quantification of admixture levels can be sensitive to the baseline reference employed.

The baseline problem: how can we be certain that the admixture of an individual is zero?

But – is the Swedish brown bear actually admixture-free? Cahill et al. (2014) found that in their data set, this individual showed the lowest amount of polar bear alleles. However, if this individual also proves to carry introgressed polar bear alleles, the admixture proportions in North American brown bears may require additional adjustment. How likely is it that polar bear alleles are found in brown bears across their range?

Mitochondrial (mt) DNA has provided evidence for at least two additional hybridization events between polar and brown bears, besides the ABC Islands case. Polar bear-like mtDNA has been found in Pleistocene fossil remains from Alaska and in now-extinct brown bears on Ireland (Edwards *et al.* 2011). This indicates that the two bear species hybridized several times over their evolutionary past. Dispersal could further distribute introgressed alleles far away from the original admixture zone.

Hence, polar bear alleles could conceivably be found in many locations across the brown bear range. This would resemble the findings from humans, where introgressed Neanderthal and Denisovan alleles have been dispersed across large distances (Sánchez-Quinto & Lalueza-Fox 2015).

Direction of introgression in polar and brown bears, and the enigmatic evolutionary history of polar bear mtDNA

One intriguing finding by Cahill *et al.* (2014) is the lack of evidence for introgression of nuclear markers into polar bears. Introgression may thus have been unidirectional, occurring only from polar into brown bears and not vice versa. Cahill and colleagues discuss how ecological factors could lead to a selective disadvantage for hybrids attempting to survive and reproduce in polar bear habitat, explaining the present findings (see also Welch *et al.* 2014).

The low effective population size of polar bears implies that ILS has a smaller impact on this species' genome, facilitating the detection of recent introgression by D and $\hat{f}$-statistics (Green *et al.*

2010; Durand *et al.* 2011). However, short coalescence times in polar bears imply that older introgression events can be missed because the introgressed alleles are likely to be fixed. Further, this statistical approach is sensitive to population structuring in the ancestral population, and can give a biased view of introgression, particularly in genomic regions that show reduced variability and/or recombination (Martin *et al.* 2015). It is therefore possible that some old introgression events transferring brown bear genetic material into polar bears might have remained undetected in the present analyses.

Interestingly, mtDNA data provide a hint that, at least during the Pleistocene, brown bear genetic material was indeed introgressed into polar bears. Brown bears are paraphyletic for mtDNA, despite their reciprocally monophyletic sister (or rather brother) lineage relationship in species trees of autosomal (Hailer *et al.* 2012, 2013; Miller *et al.* 2012; Cronin *et al.* 2014; Liu *et al.* 2014) and Y chromosomal (Bidon *et al.* 2014) markers. Based on Cahill *et al.* (2013) and Cahill *et al.* (2014), the mtDNA lineage found in brown bears on the ABC islands once arrived on the archipelago in a polar bear. This means that the extant polar bear lineage is either an 'original' polar bear lineage, or it could at some point have been introgressed from brown bears, with a loss of the original polar bear matriline.

One puzzling aspect of the contrast between mtDNA and nuclear markers is the recent divergence between polar and brown bear mtDNA lineages dates (~111-166 thousand years before present; Davison *et al.* 2011; Edwards *et al.* 2011), although the speciation likely occurred at least several 100,000 years earlier (Hailer *et al.* 2012, 2013; Miller *et al.* 2012; Cahill *et al.* 2013; Cronin *et al.* 2014). Besides ILS, and despite thorough tip calibration with fossils, underestimation of mtDNA branchings could hypothetically explain the discrepancy between divergence time estimates.

Introgression of brown bear mtDNA into polar bears during the late Pleistocene and subsequent spreading of this variant across the arctic (Edwards *et al.* 2011; Hailer *et al.* 2012) hence remains a viable hypothesis. Polar bears would then have served as a 'vector' for brown bear mtDNA, transporting it into areas as disjunct as the ABC Islands and Ireland.

The same process that has been reconstructed for the ABC Islands (Cahill *et al.* 2013, 2014) might have acted in another late Pleistocene contact zone in coastal regions – Ireland (Edwards *et al.* 2011). It would be interesting to see whether nuclear DNA can be retrieved from these Irish bear remains.

Conclusion

The study by Cahill *et al.* (2014) is an elegant demonstration of the wealth of evolutionary information that can be retrieved from the genome. Analysis of differentially inherited components of the genome – as done here for autosomes and the X chromosome - can reveal important aspects of sex-biased gene flow. In addition, the study is a reminder that, even when we have information from the entire genomes of several individuals available for analysis, another component is crucial to consider: *where (and when)* were the individuals sampled? After years of genomicists being proponents of gathering ever increasing amounts of information from single genomes for accurate parameter estimation, the field is now moving on to an old insight – different individuals capture different aspects of evolutionary history.

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Fig. 1: A brown bear in the Finnish taiga. Polar and brown bears share a complex evolutionary history - this individual might carry some polar bear DNA in its mostly brown bear-like genome. (Photo ©: Hansruedi Weyrich, www.weyrichfoto.ch)